

Figure 1A
Neutrokinin- α

1	AAATTCAAGGATAACTCTCCTGAGGGGTGAGCCAAGCCCTGCCATGTAGTGCACCGAGGAC	60
61	ATCAACAAACACAGATAACAGGAAATGATCCATTCCCTGTGGTCACTTATTCTAAAGGCC	120
121	CCAACCTTCAAAGTTCAAGTAGTAGTGATATGGATGACTCCACAGAAAGGGAGCAGTCACGCC	180
1	M D D S T E R E Q S R L	12
181	TTACTTCTTGCCCTTAAGAAAAGAGAAGAAAATGAAACTGAAGGAGTGTGTTCCATCCTCC	240
13	T S C L K K R E E M K L K E C V S I L P	32
	CD-I	
241	CACGGAAGGAAAGCCCCCTGTCCGATCCTCCAAAGACGAAAGCTGCTGGCTGCAACCT	300
33	R K E S P S V R S S K D G K L L A A T L	52
	CD-I	
301	TGCTGCTGGCACTGCTGCTTGCTGCCTCACGGTGGTGTCTTCTACCAAGGTGGCCGCC	360
53	L L A L L S C C L T V V S F Y Q V A A L	72
361	TGCAAGGGACCTGGCCAGCCTCGGGCAGAGCTGCAGGGCCACCACGCGGAGAAGCTGC	420
73	O G D L A S L R A E L Q G H H A E K L P	92
	CD-II	
421	CAGCAGGAGCAGGAGCCCCAAGGCCGGCTGGAGGAAGCCTCCAGCTGTCACCGCGGGAC	480
93	A G A G A P K A G L E E A P A V T A G L	112
	CD-III	
481	TGAAAATCTTGAAACCACCAAGCTCCAGGAGAAGGAAACTCCAGTCAGAACAGCAGAAATA	540
113	K I F E P P A P G E G N S S Q N S R N K	132
541	AGCGTGCCGTTCAAGGTCCAGAACAGTCACTCAAGACTGCTTGCAACTGATTGCAG	600
133	R A V Q G P E E T V T Q D C L Q L I A D	152
	CD-IV	
601	ACAGTGAACACCAACTATACAAAAGGATCTTACACATTGTTCCATGGCTTCTCAGCT	660
153	S E T P T I Q K G S Y T F V P W L L S F	172
	CD-V	
661	TTAAAAGGGGAAGTGCCTAGAAGAAAAAGAGAATAAAATATTGGTCAAAGAAACTGGTT	720
173	K R G S A L E E K E N K I L V K E T G Y	192
	CD-V	
721	ACTTTTTATATATGGTCAGGTTTATATACTGATAAGACCTACGCCATGGGACATCTAA	780
193	F F I Y G O V L X T P K T Y A M G H L I	212
	CD-VI	
781	TTCAGAGGAAGAAGGTCCATGTCTTGGGATGAATTGAGTCTGGTGACTTGTGTTGAT	840
213	O R K K V H V F G D E L S L V T L F R C	232
	CD-VII	
841	GTATTCAAAATATGCCTGAAACACTACCCAATAATTCCCTGCTATTCAAGCTGGCATTGCAA	900
233	I O N M P E T L P N N S C Y S A G I A K	252
	CD-VIII	
	CD-IX	

Figure 1B
Neutrokinin- α

901	AACTGGAAGAAGGAGATGA	ACTCCAAC	TTGCAATACCAAGAGAAA	ATGCACAA	ATATCAC	960
253	<u>L E E G D E L O L A I</u>	<u>P R E N A Q I S L</u>				272
	CD-X					
961	TGGATGGAGATGT	CACATTTTGGTGCATTGAA	ACTGCTGTGACCTACTTACACCATGT			1020
273	<u>D G D V T F F G A L K L L</u>					285
	CD-XI					
1021	CTGTAGCTATTTCCCTCC	TTCTGTACCTCTAAGAAGAA	AGAATCTAACTGAAAATA			1080
1081	CAAAAAA	AAAAA	AAAAA	1100		

FIGURE 2A

	10	20	30	
1	M S T E S M I R D V E L	-----	A E E A	TNFalpha
1	M -----	-----	T P P E R L	TNFbeta
1	M G A	-----	-----	LTbeta
1	M Q Q P F N Y P Y P Q I Y W	- V D S S A S S P W A P P G T V	-----	FasLigand
1	M D D S T E R E Q S R L T S C L K K R E E M K L	K E C V S I	-----	Neutrokinne alpha
1	M D D S T E R E Q S R L T S C L K K R E E M K L	K E C V S I	-----	Neutrokinne alphaSV
	40	50	60	
17	L P K K T G G P Q	G S R R	-----	TNFalpha
8	F -----	-----	-----	TNFbeta
4	----- L G L E G R G G	-----	-----	LTbeta
30	L P C P T S V P R R P G Q R R P P P P P P P P P P	L P P P P P	-----	FasLigand
31	L P R K E E S P S V R S S K D	G K L L A A T L L L A L L	-----	Neutrokinne alpha
31	L P R K E E S P S V R S S K D	G K L L A A T L L L A L L	-----	Neutrokinne alphaSV
	70	80	90	
30	-----	C L F L S L F S	-----	TNFalpha
9	----- L P R V R G T T L H L L L G L L L V I L P	-----	-----	TNFbeta
12	----- R L Q G R G S L L L A V A G A T S L V T	-----	-----	LTbeta
60	P P P L P P L P L P P L K K R G N H S T G L C L L V M F F M	-----	-----	FasLigand
58	S C C L T V V S F Y Q V A A L Q G D L A S L R A E L Q G H H	-----	-----	Neutrokinne alpha
58	S C C L T V V S F Y Q V A A L Q G D L A S L R A E L Q G H H	-----	-----	Neutrokinne alphaSV
	100	110	120	
38	F L - I V A G A T T L F C L L H F G V I G P Q R E E F P R	-----	-----	TNFalpha
31	G A Q G L P G V G L	-----	-----	TNFbeta
32	L L L A V P I T V L A V L A L V P Q D Q G G L V T E T A D P	-----	-----	LTbeta
90	V L V A L V G L G L G M F Q L F H L Q K E L A E L R E S T S	-----	-----	FasLigand
88	A E K L P A G A G A P K A G L E E A P A V T A G L K I F E P	-----	-----	Neutrokinne alpha
88	A E K L P A G A G A P K A G L E E A P A V T A G L K I F E P	-----	-----	Neutrokinne alphaSV
	130	140	150	
66	D L S L I S - P L A - Q A V R S S S R T P S D	-----	K P V A	TNFalpha
41	----- T P S - A A Q - T A R Q H P K M H L A H S T L K P A A	-----	-----	TNFbeta
62	G A Q A Q Q - G L G F Q K L P E E E P E T D L S P G L P A A	-----	-----	LTbeta
120	Q M H T A S - S L E - K Q I G H P S P P P E K K E L R K V A	-----	-----	FasLigand
118	P A P G E G N S S O N S R N K R A V Q G P E E T V T Q D C L	-----	-----	Neutrokinne alpha
118	P A P G E G N S S O N S R N K R A V Q G P E E T	-----	-----	Neutrokinne alphaSV
	160	170	180	
91	H V V A N P Q A E G - Q	-----	L Q W L N R R A N A L L	TNFalpha
66	H L I G D P S K Q N - S	-----	L L W R A N T D R A F L	TNFbeta
91	H L I G A P L K - G Q G	-----	L G W E T T K E Q A F L	LTbeta
148	H L T G K S N S R S M P	-----	L E W E D T Y G I V L L	FasLigand
148	Q L I A D S E T P T I Q K G S Y T F V P W L	-----	L S F K	Neutrokinne alpha
142	----- G S Y T F V P W L	-----	L S F K	Neutrokinne alphaSV

FIGURE 2B

	190	200	210	
114	A N G V E L R D N - Q L V V P S E G L Y L I Y S Q V L F K G			TNFalpha
89	Q D G F S L S N N - S L L V P T S G I Y F V Y S Q V V F S G			TNFbeta
114	T S G T Q F S D A E G G L A L P Q D G L Y Y L Y C L V G Y R G			L1beta
172	- S G V K Y K K G - G L V I N E T G L Y F V Y S K V Y F R G			FasLigand
174	R G S A L E E E K E N K I L V K E T G Y F F I Y G Q V L Y T D			Neutrokinne alpha
155	R G S A L E E E K E N K I L V K E T G Y F F I Y G Q V L Y T D			Neutrokinne alphaSV
	220	230	240	
143	Q G C P - - - - S T H V L L T H T I S R I A V S Y Q T K			TNFalpha
118	K A Y S P - - K A T S S P L Y L A H E V Q L F S S Q Y P F H			TNFbeta
144	R A P P G G G D P Q G R S V T L R S S L Y R A G G A Y G P G			L1beta
200	Q S C N - - - - N L P L S H K V Y M R N S K Y P Q D			FasLigand
204	K T Y A M G - - - - H L I Q R K K V H V F G D E L S - -			Neutrokinne alpha
185	K T Y A M G - - - - H L I Q R K K V H V F G D E L S - -			Neutrokinne alphaSV
	250	260	270	
167	V N - - L L S A I K S P C Q R E T P E - - G A E A K P W Y E			TNFalpha
146	V P - - L L S S Q K M V Y P - - - - G L Q E P W L H			TNFbeta
174	T P E L L L E G A E T V T P V L D P A R R Q G Y G P L W Y T			L1beta
222	L V - - M M E G K M M S Y C - - - - T T G Q M W A R			FasLigand
226	L V T L F R C I Q N M P E T L P N - - - - - - - - N			Neutrokinne alpha
207	L V T L F R C I Q N M P E T L P N - - - - - - - - N			Neutrokinne alphaSV
	280	290	300	
193	P I Y L G G V F Q L E K G D R L S A E I N R P D Y L D F A E			TNFalpha
166	S M Y H G A A F Q L T Q G D Q L S T H T D G I P H L V L S P			TNFbeta
204	S V G F G G L V Q L R R G E R V Y V N I S H P D M V D F A R			L1beta
242	S S Y L G A V F N L T S A D H L Y V N V S E L S L V N F E E			FasLigand
244	S C Y S A G I A K L E E G D E L Q L A I P R E N A Q I S L D			Neutrokinne alpha
225	S C Y S A G I A K L E E G D E L Q L A I P R E N A Q I S L D			Neutrokinne alphaSV
	310			
223	S G Q V Y F G I I A L			TNFalpha
196	S - T V F F G A F A L			TNFbeta
234	- G K T F F G A V M V G			L1beta
272	S - Q T F F G L Y K L			FasLigand
274	G D V T F F G A L K L L			Neutrokinne alpha
255	G D V T F F G A L K L L			Neutrokinne alphaSV

Figure 3
Neutrokinin- α

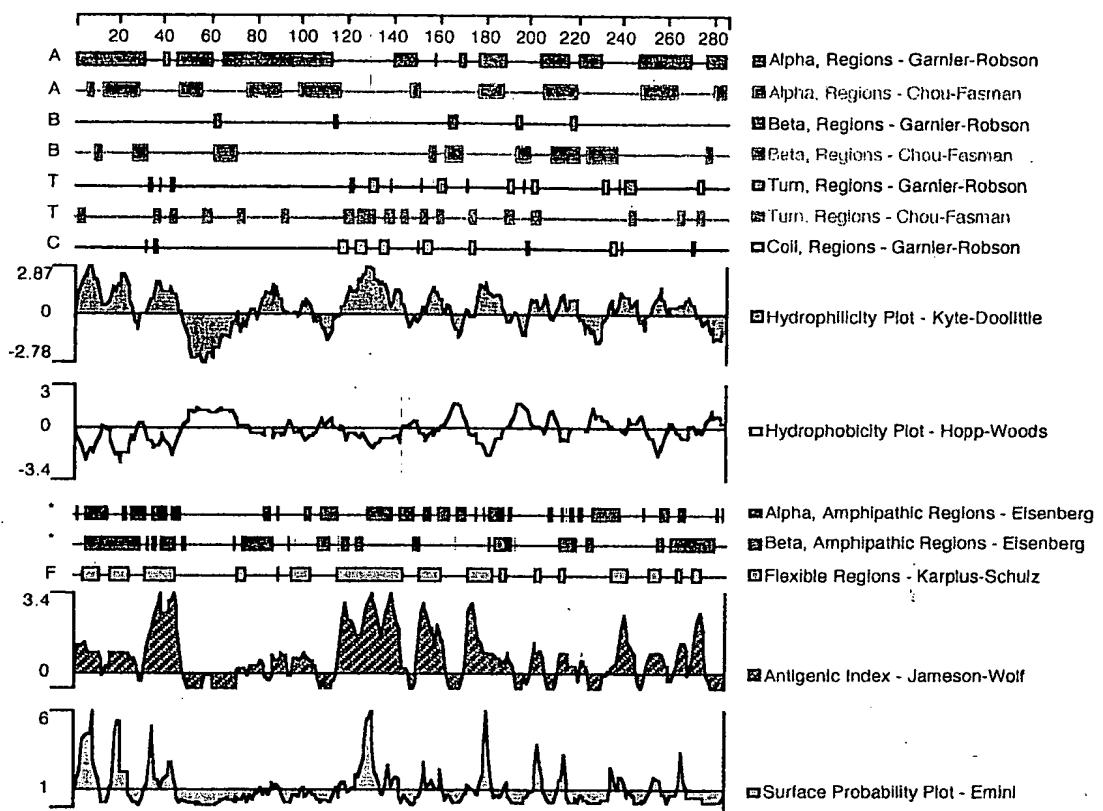


FIGURE 4 A

1	50
HSOAD55RA GGNTAACTCT CCTGAGGGGT GAGCCAAGCC CTGCCATGTA
HNEDU15X	...AAATTCA GGATAACTCT CCTGAGGGGT GAGCCAAGCC CTGCCATGTA
HSLAH84R	.AATTGGCA NAGNAAACTG GTTACTTTT TATATATGGT CAGGTTTAT
HLTBM08R	AATTGGCAC GAGCAAGGCC GGCTGGAGG AAGCTCCAGC TGTCACCGCG
51	
HSOAD55R	GTGCACGCAG GACATCANCA A..ACACANN NNNCAGGAAA TAATCCATT
HNEDU15X	GTGCACGCAG GACATCAACA A..ACACAGA TAACAGGAAA TGATCCATT
HSLAH84R	ATACTGATAA GACCTACGCC ATGGGACATC TAGTCAGAG GAAGAAGGTC
HLTBM08R	GGACTGAAAA TCTTGAAACC ACCAGCTCCA GGAGAAGGCA ACTCCAGTCA
101	
HSOAD55R	CCTGTGGTCA CTTATTCTAA AGGCCCAAC CTTCAAAGTT CAAGTAGTGA
HNEDU15X	CCTGTGGTCA CTTATTCTAA AGGCCCAAC CTTCAAAGTT CAAGTAGTGA
HSLAH84R	CATGTCTTG GGGATGAATT GAGTCTGGTG ACTTTGTTTC GATGTATTCA
HLTBM08R	GAACAGCAGA AATAAGCGTG CCGTTCAGGG TCCAGAAGAA ACAGTCACTC
151	
HSOAD55R	TATGGATGAC TCCACAGAAA GGGAGCAGTC ACGCCTTA TCTTGCTTA
HNEDU15X	TATGGATGAC TCCACAGAAA GGGAGCAGTC ACGCCTTA TCTTGCTTA
HSLAH84R	AAATATGCCT GAAACACTAC CCAATAATTCA CTGCTATTCA GCTGGCATTG
HLTBM08R	AAGACTGCTT GCAACTGNTT GCAGACAGTG AAACACCAAC TATACAAAAA
201	
HSOAD55R	AGAAAAGAGA AGAAATGAAA CTGNAAGGAG TGTGTTCCA TCCTCCACG
HNEDU15X	AGAAAAGAGA AGAAATGAAA CT.GAAGGAG TGTGTTCCA TCCTCCACG
HSLAH84R	CAAAACTGGN AGGAAGGA... GATGAAC TCCAACTTGC AATACCAGGG
HLTBM08R	GGCTCCCTTC TGNTGCCACA TTTGGGCCAA GGAATGGAGA GATTCTTCG
251	
HSOAD55R	GAAGGAAAGC CCCTCTNTCC GATCCTCCAA AGACGGAAAG CTGCTGGCTG
HNEDU15X	GAAGGAAAGC CCCTCTGTCC GATCCTCCAA AGACGGAAAG CTGCTGGCTG
HSLAH84R	GAAAATGCAC AATTATCACT GGGATGGAGA TGTTCACATT TTTGGGTGC
HLTBM08R	TCTGGAAACA TTTGCCAAA CTCTTCAGAT ACTCTTNCT CTCTGGGAAT
301	
HSOAD55R	CAACCTTGNT GNTGGCATTG TGTCTTGCT GNCTCAAGGT GGTGTTNTT.
HNEDU15X	CAACCTTGCT GCTGGCACTG CTGTCTTGCT GCCTCACGGT GGTGTTTC
HSLAH84R	CATTGAAACT GCTGTGACCT NCTTACANCA NGTGTGTTN GCTATTTNC
HLTBM08R	CAAAGGAAAA TCTCTACTTA GATTNACACA TTTGTCCCA TGGGTNTCTT
351	
HSOAD55R
HNEDU15X	TACCAAGGTGG CCGCCCTGCA AGGGGACCTG GCCAGCCTCC GGGCAGAGCT
HSLAH84R	CTNCCTNTTC TNTGGTAACC TCTTAGGAAG GAAGGATTCT TAACTGGAA
HLTBM08R	AAGTTTAAA AGGGGAGTGC CCTTAGGAGG AAAAGGGAT AAATATTGGC

FIGURE 4B

	401	450
HSOAD55R	
HNEDU15X	GCAGGGCCAC CACGCCGAGA AGCTGCCAGC AGGAGCAGGA GCCCCCAAGG	
HSLAH84R	ATAACCCAAA AAAANNTAA ANGGGTANGN GNNANANGNG GGGNNNGTNN	
HLTBM08R	CAAGGNACTG GTTANTTTNT AAATATGGTC AGGTTNTAT ANCTGGTAGG	
	451	500
HSOAD55R	
HNEDU15X	CCGGCCTGGA GGAAGCTCCA GCTGTCACCG CGGGACTGAA AATCTTGAA	
HSLAH84R	CNNGNNGNNNT TTTNGGNNTA TNTTNTNNNT GGGNNNNGTA AAAATGGGC	
HLTBM08R	CCTCGCCATG GGCATTNATT CANGGNAGGG NCNNCTTTT GGGNTGA...	
	501	550
HSOAD55R	
HNEDU15X	CCACCAGCTC CAGGAGAAGG CAACTCCAGT CAGAACAGCA GAAATAAGCG	
HSLAH84R	CNANGGGGN TTTTT.....	
HLTBM08R	
	551	600
HSOAD55R	
HNEDU15X	TGCCGTTCAAG GGTCCAGAAG AAACAGTCAC TCAAGACTGC TTGCAACTGA	
HSLAH84R	
HLTBM08R	
	601	650
HSOAD55R	
HNEDU15X	TTGCAGACAG TGAAACACCA ACTATACAAA AAGGATCTTA CACATTTGTT	
HSLAH84R	
HLTBM08R	
	651	700
HSOAD55R	
HNEDU15X	CCATGGCTTC TCAGCTTAA AAGGGGAAGT GCCCTAGAAG AAAAAGAGAA	
HSLAH84R	
HLTBM08R	
	701	750
HSOAD55R	
HNEDU15X	TAAAATATTG GTCAAAGAAA CTGGTTACTT TTTTATATAT GGTCAGGTTT	
HSLAH84R	
HLTBM08R	
	751	800
HSOAD55R	
HNEDU15X	TATATACTGA TAAGACCTAC GCCATGGGAC ATCTAATTCA GAGGAAGAAG	
HSLAH84R	
HLTBM08R	

FIGURE 4C

	801	850
HSOAD55R
HNEDU15X	GTCCATGTCT TTGGGGATGA ATTGAGTCTG GTGACTTTGT TTCAATGTAT	
HSLAH84R
HLTBM08R
	851	900
HSOAD55R
HNEDU15X	TCAAAATATG CCTGAAACAC TACCCAATAA TTCTGCTAT TCAGCTGGCA	
HSLAH84R
HLTBM08R
	901	950
HSOAD55R
HNEDU15X	TTGCACAAACT GGAAGAAGGA GATGAACCTCC AACTTGCAAT ACCAAGAGAA	
HSLAH84R
HLTBM08R
	951	1000
HSOAD55R
HNEDU15X	AATGCACAAA TATCACTGGA TGGAGATGTC ACATTTTTG GTGCATTGAA	
HSLAH84R
HLTBM08R
	1001	1050
HSOAD55R
HNEDU15X	ACTGCTGTGA CCTACTTACA CCATGTCTGT AGCTATTTTC CTCCCTTTCT	
HSLAH84R
HLTBM08R
	1051	1100
HSOAD55R
HNEDU15X	CTGTACCTCT AAGAAGAAAG AATCTAACTG AAAATACCAA AAAAAAAA	
HSLAH84R
HLTBM08R
	1101	
HSOAD55R	
HNEDU15X	AAAAAA	
HSLAH84R	
HLTBM08R	

Figure 5A
Neutrokinin- α SV

1	ATGGATGACTCCACAGAAAGGGAGCAGTCACGCCCTACTTCTTGCCTTAAGAAAAGAGAA	60
1	M D D S T E R E Q S R L T S C L K K R E	20
61	GAAATGAAACTGAAGGAGTGTGTTCCATCCTCCACGGAAAGGAAAGCCCTCTGTCCGA	120
21	E M K L K E C V S I L P R K E S P S V R	40
	CD-I	
121	TCCTCCAAAGACGGAAAGCTGCTGGCTGCAACCTTGTGCTGGCACTGCTGTCTGCTGC	180
41	<u>S S K D G K L L A A T L L L A L L S C C</u>	60
	CD-I	
181	CTCACGGTGGTGTCTTCTACCAAGGTGGCCGCTGCAAGGGGACCTGCCAGCCTCCGG	240
61	<u>L T V V S F Y Q V A A L Q G D L A S L R</u>	80
	CD-II	
241	GCAGAGCTGCAGGGCACCACGGAGAACGCTGCCAGCAGGAGCAGGAGCCCCAAGGCC	300
81	<u>A E L Q G H H A E K L P A G A G A P K A</u>	100
	CD-II	
	CD-III	
301	GGCCTGGAGGAAGCTCCAGCTGTCACCGCGGGACTGAAATCTTGAACCACAGCTCA	360
101	<u>G L E E A P A V T A G L K I F E P P A P</u>	120
	CD-III	
	#	
361	GGAGAAGGCAACTCCAGTCAGAACAGCAGAAATAAGCGTGGCTCAGGGTCCAGAAGAA	420
121	<u>G E G N S S Q N S R N K R A V Q G P E E</u>	140
421	ACAGGATCTTACACATTGTTCCATGGCTCTCAGCTTAAAAGGGGAAGTGCCCTAGAA	480
141	<u>T G S Y T F V P W L L S F K R G S A L E</u>	160
	CD-IV	
481	GAAAAAGAGAATAAAATATTGGTCAAAGAAACTGGTTACTTTTATATATGGTCAGGTT	540
161	<u>E K E N K I L V K E T G Y F F I Y G O V</u>	180
	CD-IV	
	CD-V	
541	TTATATACTGATAAGACCTACGCCATGGACATCTAATTCAAGAGGAAGAGTCATGTC	600
181	<u>L Y T D K T Y A M G H L I O R K K V H V</u>	200
	CD-VI	
	CD-VII	
601	TTGGGGATGAATTGAGTCTGGTACTTGTGATGTATTCAAATATGCCCTGAAACA	660
201	<u>F G D E L S L V T L F R C I O N M P E T</u>	220
	CD-VIII	
	CD-VIII	
661	CTACCCATAATTCTGCTATTCACTGGCATGCCAAACTGGAAGAAGGAGATGAACATC	720
221	<u>L P N N S C Y S A G I A K L E E G D E L</u>	240
	CD-IX	
	CD-X	
721	CAACTTGAATACCAAGAGAAAATGCACAAATATCACTGGATGGAGATGTCACATT	780
241	<u>Q L A I P R E N A Q I S L D G D V T F F</u>	260
	CD-X	
	CD-XI	
781	GGTGCATTGAAACTGCTGTGACCTACTTACACCATGTCTGTAGCTATTTCCCTCCCTTC	840
261	<u>G A L K L L</u>	266
	CD-XI	

Figure 5B
Neutrokin- α SV

841 TCTGTACCTCTAAGAAGAAGAATCTAACTGAAATACCAAAAAAAAAAAAAA 900
901 AAA 903

Figure 6
Neutrokinin- α SV

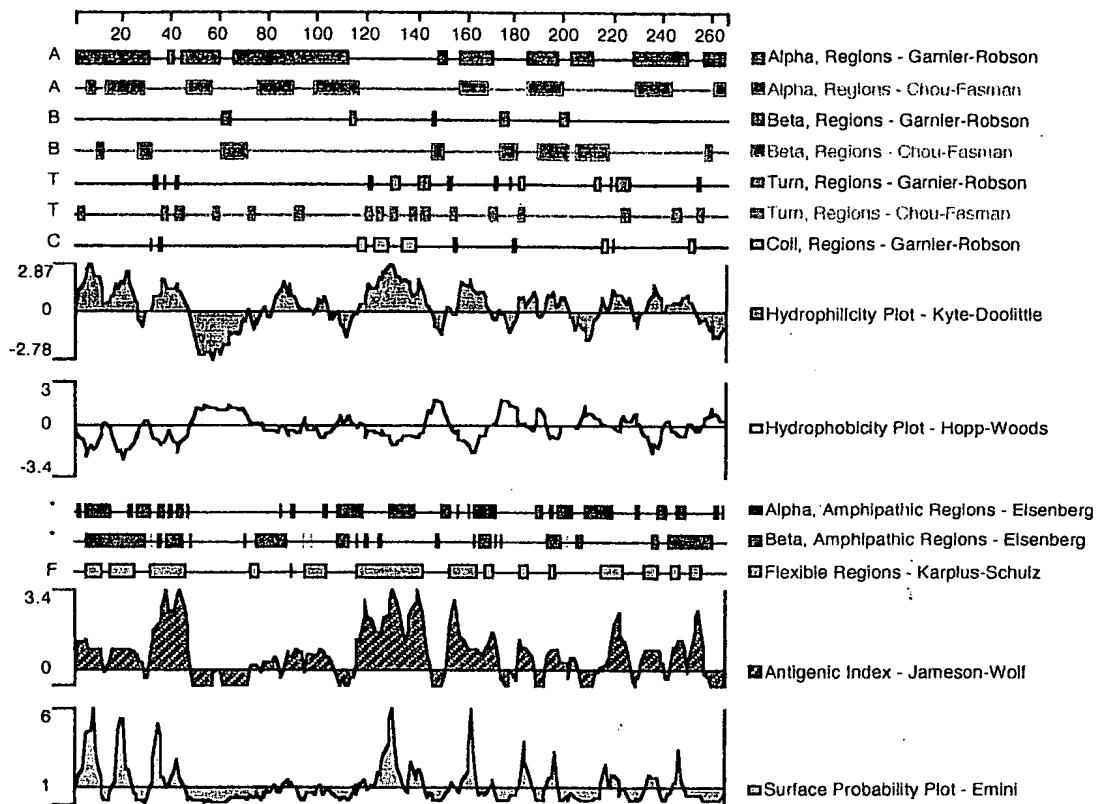


Figure 7

a.

leukotriene-

alpha M D D S T E R E Q S R L T S C L K K R E E M K L K E C V S I L P R K E S P S V R S 41

Transmembrane Region

S K D G K L L A A T L L I L L S C C L T V V S F Y Q V A A L Q G D L A S L R A E 82

L Q G H H A E K L P A G A G A P K A G L E A P A V T A G L K I F E P P A P G E G 123

↓

	A	B	C	D	E	F	G
N S S Q N S R N K R A V Q G P E E T V T Q D C D Q D T R A D S E P T I Q K G S Y	164						
April H S V D H S D V P I N A S K - D D S D V	134						
TNF K P Q A H V V E N P Q A E G Q - - - - -	102						
LT α K P Q A H V E N P S K Q N S - - - - -	77						
F P D L S - - - - - F K R G S A P E E K E N K I E M K E T G Y F P H Y G R O V I	200						
E K M Q P A - - - - - R A G R G E Q A Q G Y G V R I Q D A G V V L L E S S V E	170						
- L Q T N R R A N L A N G V E E R D - - - Q T V V P S E C G L L L P Y S O V V	139						
- L L W R A N T D R F Q D G F S S N - - - S E L V E T S C O I P V V Y S O V V	114						
Y T D I E T V - - - - - A M C H E I Q R K K V H V E G D E L S L V D I I C I C I O N M P P	237						
Q D E V F - - - - - A E M V Q V V S E - - - - - G D G G R Q E T D I R G H R S M P P	201						
K G Q G C P - - - - - S T P V L H T E T I S R I A V S S Q N Q T K V N L L S A I K S M P P	176						
S G K A W S P K A Q S S P H Y A H E V Q L E S S Q N P F H V P L L S S O K M V	155						
E - - T L E - - - - - N N S C Y S A G I A K E E G D E E Q L A T P R E N M P P	268						
S H P D R A - - - - - V N N S C Y S A G V E H H H D G D I E V I T P R A R M P P	234						
C Q R E T E E G A E A K P W M E P I N L G G V I E Q L E K G D R E G A E E N R P D Y M P P	217						
Y P - - - - - G L Q E A W L H C M H G A A E Q H T D G D Q T H T D G I P H M P P	190						
Q I S D G D V D P F R G A L K E L	285						
K L N S H G D L G F V K	250						
D F A E S S G Q V Y E G I I A	233						
V L S I S T V F P G F F A	205						

b.

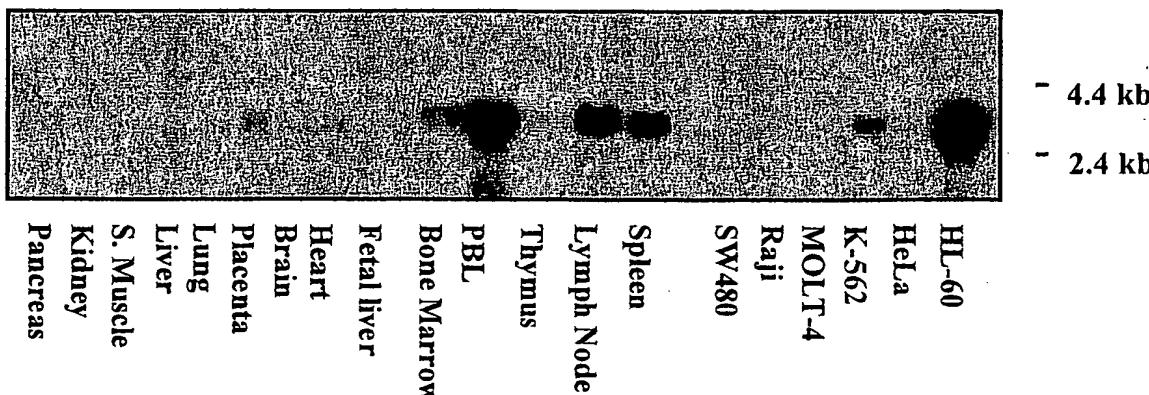
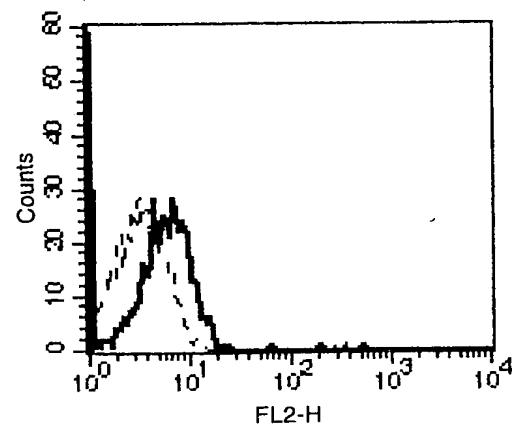


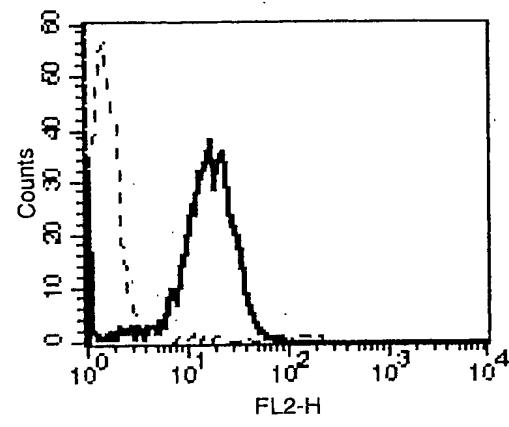
Figure 8

a.

Medium only



IFN γ (100 U/mL)



b.

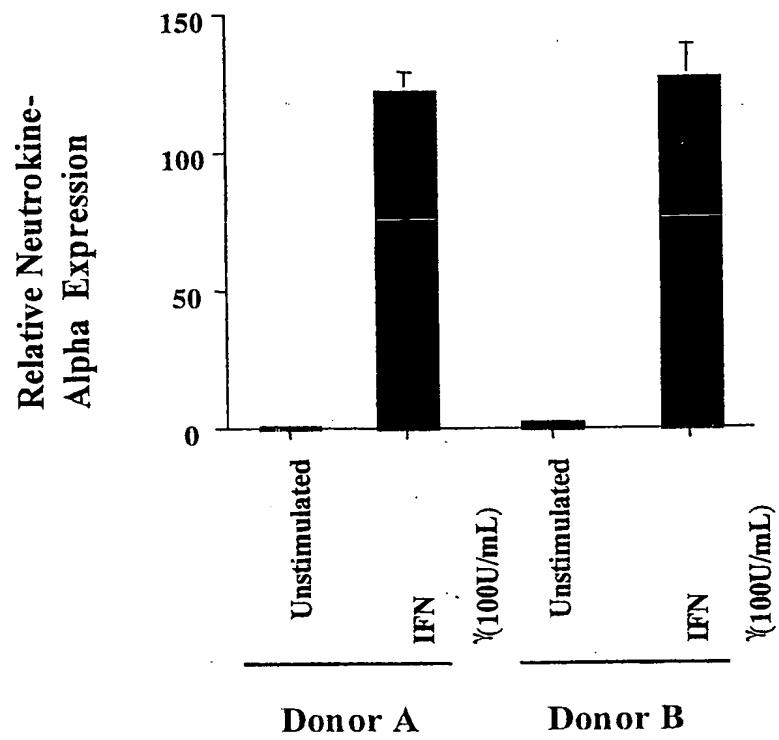
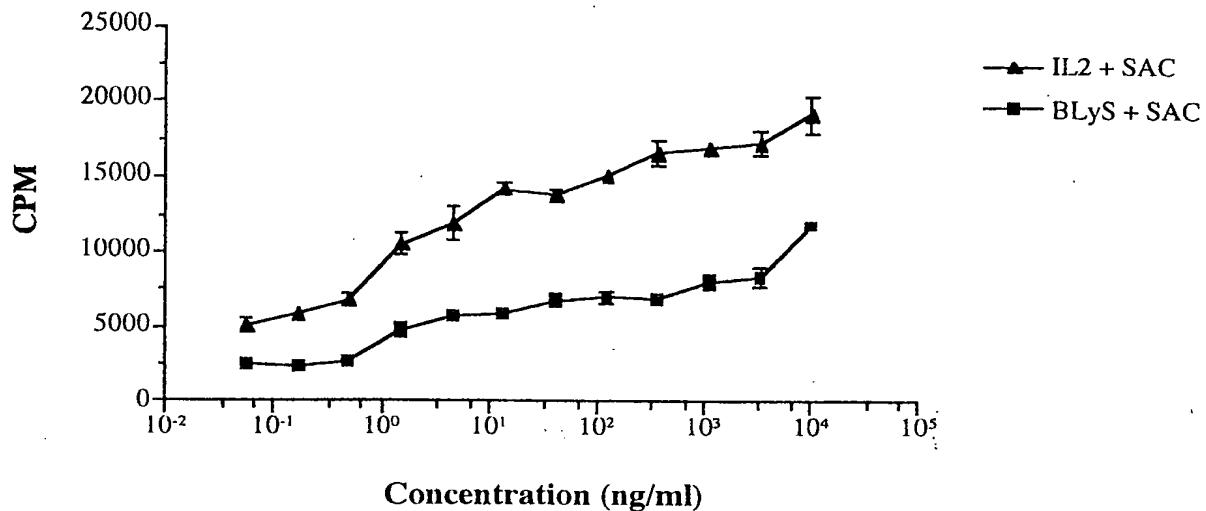


Figure 9

a.



b.

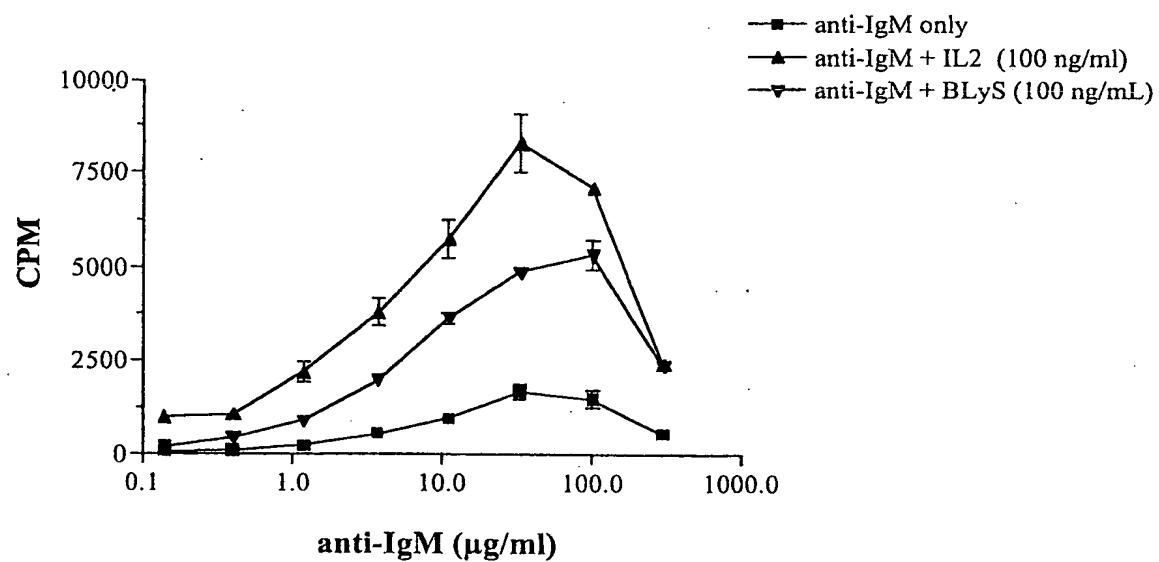
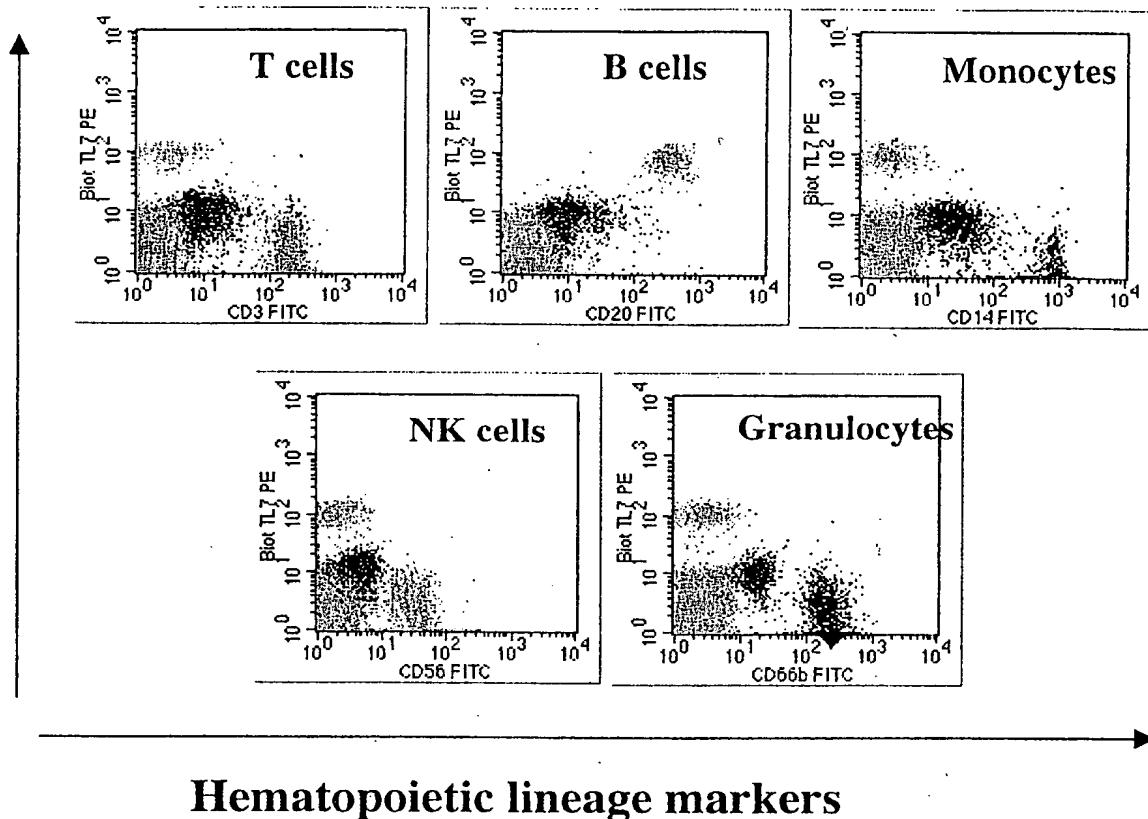


Figure 10

**Biotinylated Neutrokinine-
alpha binding**

a.



Hematopoietic lineage markers

b.

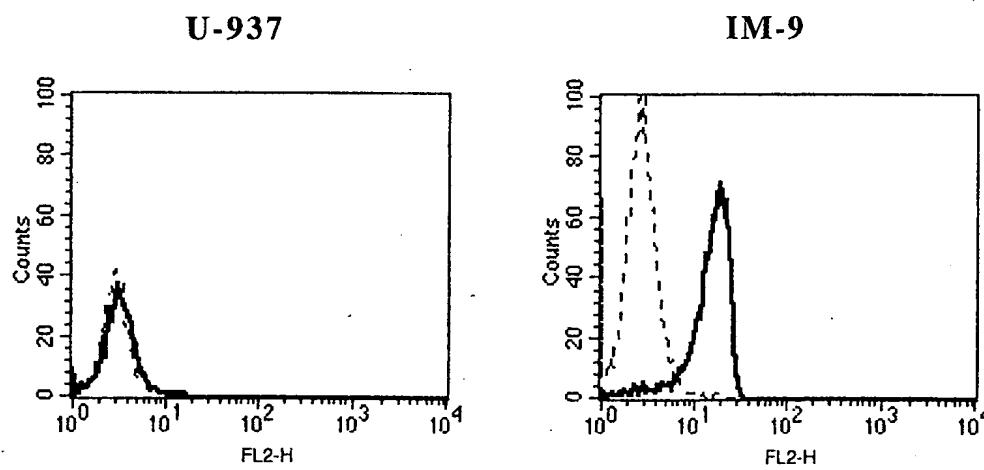


Figure 11

